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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,643	03/17/2004	Paul Noel Holvoet	91752CON1	3956

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,643	HOLVOET ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/17/04; 6/18/04;*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continuing Application

1. The request filed on 3/17/04 for a Continuation under 37 CFR 1.53(b) based on parent Application No. 09/446,259 is acceptable. An action on the Continuation follows.

Preliminary Amendment

2. Applicants' amendment filed 3/17/04 is acknowledged. All previous claims have been canceled. New claims 56-74 were added. Currently claims 56-74 are pending and under consideration.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

4. The Information Disclosure Statements filed on 3/17/04, 6/18/04, 6/23/04, and 11/10/05 were considered as to the merits prior to first Acton.

Specification

5. The disclosure is objected to because of the following informalities: Page 1 of the disclosure should be updated to include US Patent #6,727,102. Appropriate correction is required.

Double Patenting

6. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 56- 74 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-54 of US Patent #6,309,888. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims are drawn to the detection of MDA-modified and human OxLDL in a sample.

Claims 1-54 in US Patent #6,309,888 detects multiple markers in the claimed method, however the measurement of additional markers is encompassed by the single marker method recited in the instant application. Further, both methods utilizing the same reagents. (mAb-8A2, mAb-1H11, mAb-4E6).

The limitations recited in the preamble of claims 1-54 in US Patent #6,309,888 are not given patentable weight. The intended use of the method is not germane to the issue of patentability of the method itself. Therefore, this limitation has not been given patentable weight.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 56 is rejected under 35 U.S.C. 102(b) as being anticipated by Holvoet et al. (Journal of Clinical Investigation, Vol.95., No.6., 1 June 1995, pages 2611-2619)

Holvoet et al. disclose a method for detecting MDA-modified LDL. A monoclonal antibody (mAb-1H11) which to bind with MDA-modified LDL (ka=10^9 M^{-1}) and to a much lesser extent with OxLDL (page 2613, column 2, paragraph 1) is described in an immunoassay format.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 57-71 and 73-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holvoet et al. (Journal of Clinical Investigation, Vol.95., No.6., 1 June 1995, pages 2611-2619) in view of Kondo, Akira et al. (EPO 0 484 863 A1).

Please see Holvoet et al as set forth above.

Holvoet et al. differ from the instant invention in not teaching antibodies directed to various MDA-modified LDL and OxLDL molecules having different lysine moiety compositions and different affinity constants.

Kondo et al. teach a monoclonal antibody and a sandwich immunoassay for measuring malondialdehyde-modified LDL. (See Abstract, Page 4, lines 9-32, Example 5).

Example 5 teaches a sandwich assay-utilizing antibody 290209 which was generated against and reacted with MDA-modified LDL (Table 1, Page 5, Lines 38-42). The assays comprise the steps of a) binding the first antibody to the substrate (polystyrene ball) and reacting it with human MDA-modified LDL, b) thoroughly washing, c) contacting the complex with peroxidase-labelled anti-apo B antibody and d) visualizing the MDA-modified LDL by the enzymatic reaction with hydrogen peroxide, orthophenylendiamine as substrates. The second antibody (anti-apo B) has a high affinity to the apo B 100 molecules, which is the predominant apolipoprotein on MDA-modified LDL. The conditions of the sandwich assay are such that the anti apo B antibody can only react with MDA-modified LDL, as all other LDL of the original sample are washed in step b).

The preparation of the MDA-modified LDL according to the reference of Kondo et al. does not differ significantly from the preparation according to the instant invention.

Therefore there is no hint that the two methods could lead to different MDA-modified LDL. Consequently, the antibodies raised against these MDA-modified LDL should also not differ significantly. In addition the sensitivity of the antibodies found in the reference of Kondo et al., in particular No 29210 is at least as high as the sensitivity of antibodies according to the present application.

Antibody 29210 disclosed by Kondo et al., shows a detection limit of less than 0.01 mg/dl MDA modified LDL in an ELISA (Example 4, figure 5). The antibody of the present application is capable of detecting 0.02 mg/dl of MDA-modified LDL in a competitive ELISA (disclosure page 17, lines 1-2).

Moreover, the MDA-modified LDL for which the first and second antibody has high affinity contains at least 60 substituted lysine residues per apo B-100 molecule. The antibody 29209 has a high affinity for invitro MDA-modified LDL.

Therefore, One of ordinary skill in the art would produce and utilize various comparative antibody constructs directed to different lysine moieties having diverse binding affinity to detect MDA-modified LDL and OxLDL in a test sample such modifications for the resulting data sets to evaluated and detect different forms of MDA-modified LDL and OxLDL are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to employ different antibodies with different specificity to MDA-modified LDL and OxLDL in the given parameters to determine the unknown as a means of optimizing the assays provided by the art.

One of ordinary skill would have been motivated to do this because Kondo et al taught that modified-LDL exits in two forms – chemically oxidized LDL by copper ions and MDA. Clearly a precise measurement of modified forms of LDL would encompass the detection of both forms. See page 2, lines 24-31.

10. For reasons aforementioned, no claims are allowed.

Remarks

11. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Selley et al. (WO 94/23302) teach an immunological ELISA assay-employing antibodies to measure oxidatively modified human low-density lipoproteins in plasma samples.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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January 8, 2006

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01/20/06